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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,134	02/11/2005	Scott Koenig	11183-003-999	1503
20583	7590	04/10/2006	EXAMINER	
JONES DAY 222 EAST 41ST ST NEW YORK, NY 10017			CROWDER, CHUN	
			ART UNIT	PAPER NUMBER
			1644	
DATE MAILED: 04/10/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)	
10/524,134	KOENIG ET AL.	
Examiner	Art Unit	
Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 30 January 2006.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-109 is/are pending in the application.
4a) Of the above claim(s) 2-8,22,24-29,33-37,39,40,44-80 and 91-103 is/are withdrawn from consideration.
5) Claim(s) _____ is/are allowed.
6) Claim(s) 1, 9-21, 23, 30-32, 38, 41-43, 81-90, 104-109 is/are rejected.
7) Claim(s) _____ is/are objected to.
8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ .

5) Notice of Informal Patent Application (PTO-152)

6) Other: *See Continuation Sheet.*

Continuation of Attachment(s) 6). Other: Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures..

DETAILED ACTION

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

An amino acid sequence is disclosed on page 12 of the instant specification. However, the sequence fails to comply with the Sequence Rules.

Applicant is reminded of the Sequence Rules which require a submission for all sequences of 10 or more nucleotides or 4 or more amino acids (see 37 CFR 1.1821-1.1825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules.

Applicant must comply with the requirements of the Sequence Rules (37 CFR 1.1821-1.1825) in response to this Office Action.

2. Applicant's election with traverse of Group II and species of antibody 2B6 without conjugation, filed 01/30/2006, is acknowledged.

The traverse is on the ground that Groups I and II have a special technical feature over the prior art teachings of Presta in that the instant inventions teaches the variable domains of the antibody are responsible for binding to the antigen while Presta teaches modified Fc region of an antibody that has altered binding to Fc receptors.

This is not found persuasive because the originally presented claims lack the same or corresponding special technical feature that is a contribution over the prior Presta for the reasons set forth in the Office Action mailed 11/30/2005.

In addition, the newly amended claims contain inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2, they lack the same or corresponding special technical features over prior art of Weinrich et al. (Hybridoma. 1996, 15;2:109-116. Reference C68 in IDS) for the reasons stated in paragraph 11 of this Office Action.

Therefore, the restriction requirement is still deemed proper and is made FINAL.

Claims 1, 23, 39, 42, 81-90, and 105 have been amended.

Claims 108 and 109 have been added.

Claims 1-109 are pending.

Claims 2-8, 22, 24-29, 33-37, 39, 40, 44-80, 91-103 have been withdrawn from further consideration by the Examiner, under 37 C.F.R. 1.142(b), as being drawn to nonelected inventions.

Claims 1, 9-21, 23, 30-32, 38, 41-43, 81-90, 104-109, read on an isolated antibody of clone 2B6 without conjugation that binds to native Fc γ RIIB with greater affinity than Fc γ RIIA and antagonizes at least one activity of Fc γ RIIB, is currently under consideration.

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) and 35 U.S.C. 371 is acknowledged. The priority applications PCT/US03/25399 and 60/403,266 upon which benefit is claimed appear to provide adequate support under 35 U.S.C. 112 for subject matter claimed in the instant application.

The specification on page 1, line 1 should include a specific reference to the priority application PCT/US03/25399 for which benefit is sought and the status of the instant application is a 371.

4. Applicant's IDS, filed 07/15/2005, is acknowledged and considered.
5. The application is required to be reviewed and all spelling, TRADEMARK, and like error corrected.

Trademarks should be capitalized or accompanied by the TM or [®] symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent application, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
7. Claims 9, 12, 31, 41, and 109 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 9 and 14 are indefinite in the recitation of "at least one activity of FcγRIIB" and "B cell activity", respectively, because the metes and bounds of the activities is not clear and ambiguous. For example, pages 14 and 30 of the specification disclose certain "activities of FcγRIIB" and "B cell activities", respectively, however, it is unclear as to which "activities" or the requisite structural/functional characteristic is/are intended or encompassed by the claimed antibody.

It is suggested to amend the claims to recite the “activities of Fc γ RIIB” and/or “B cell activity” encompassed by the claimed antibody. See claim 13 for example.

B) Claim 31 is indefinite in the recitation of “immune response” because the metes and bounds of the “immune response” is not clear and ambiguous. For example, page 14 of the specification discloses certain “immune response”; however, it is unclear as to which “immune response” or the requisite structural/functional characteristic is/are intended or encompassed by the claimed antibody.

It is suggested to amend the claims to recite the “immune response” encompassed by the claimed antibody. See claim 32 for example.

C) Claim 41 are indefinite in the recitation of ““humanized”. There is insufficient antecedent basis for this limitation in this claim. The clone 2B6 produces a monoclonal antibody, not a humanized antibody.

Applicant is suggested to amend the preamble of the claim to include “humanized antibody” and recite the source of the antibody accordingly.

D) Claim 109 is indefinite in the recitation of “denatured Fc γ RIIB” because the metes and bounds of “denature” is unclear and ambiguous. The phrase is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonable apprised of the metes and bounds of the invention.

E) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

Art Unit: 1644

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 38, 41-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the **hybridoma 2B6 that produces the mouse monoclonal antibody** is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, a deposit of the **hybridoma 2B6**, which produces this antibody, may satisfy first paragraph. See 37 CFR 1.801-1.809.

Applicant discloses on page 29 of the instant specification that hybridoma 2B6 producing the claimed antibody has been deposited with ATCC under Budapest Treaty on 08/13/2002. In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in US patent applications.

An affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the **hybridoma** has been deposited under the Budapest Treaty and that the **hybridoma will be irrevocably and without restriction or condition released to the public upon the issuance of a patent** would satisfy the deposit requirement made herein. See 37 CFR 1.808.

Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample *or for the enforceable life of the patent whichever is longer*. See 37 CFR 1.806.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 9-16, 23, 30-32, 81-90, 108, and 109 are rejected under 35 U.S.C. 102(b) as being anticipated by Weinrich et al. (Hybridoma. 1996, 15:2:109-116. Reference C68 in IDS) (See entire document) as evidenced by Bolland et al. (Advances in Immunology. 1999. 72:149-177. Reference C04 in IDS) (See entire document) and Clynes et al. (Nature Medicine. 2000. 6:4:443-446. Reference C15 in IDS) (See entire document).

Weinrich et al. teach that a monoclonal antibody II8D2, made from mice immunized with recombinant Fc γ RIIB, is specific for Fc γ RIIB without cross-reactivity with Fc γ RIIA in phosphate buffered saline based ELISA (see entire document, particularly Material and Method on pages 110-111 and Results on pages 111-114). Weinrich et al. further teach that the anti-Fc γ RIIB antibody can be used to detect Fc γ RIIB on B cell line Daudi.

As evidenced by Bolland et al, crossing linking Fc γ RIIB antagonizes Fc γ RIIB activities such as B cell receptor-mediated signaling involving signaling molecules including Btk kinase, PLC γ , PI3 kinase, and SHIP (see entire document, particularly pages 154-156). Further, Bolland et al. teach that in addition to the inhibitory function on B cell activation, Fc γ RIIB can also inhibit FcR-triggered mast cell degranulation involving Fc ϵ RI (e.g. see page 157-158, in particular).

As further evidenced by Clynes et al, Fc γ RIIB is a potent regulator of antibody-dependent cell-mediated cytotoxicity (ADCC) and optimal antibody against tumors that binds less to Fc γ RIIB and more to Fc γ RIII would enhance ADCC (see entire document, particularly pages 444-445).

Given the properties of the prior art the Fc γ RIIB specific antibody; the claimed functional limitations would be inherent properties of the antibody. Also, the Courts have held that there is no requirement that those of ordinary skill in the art know of the inherent property. See MPEP 2131.01(d) and MPEP 2112-2113 for case law on inherency.

When claims recite using an old composition or structure (e.g. anti-Fc γ RIIB antibody) and the use is directed to a result or property of that composition or structure, then the claims are anticipated. See MPEP 2112.02. Also, see Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Therefore, the reference teachings anticipate the claimed invention.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 1 and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reff et al. (Critical Review in Oncology/Hematology. 2001. 40:25-35) in view of Ott et al. (J. Allergy Clin. Immunol. 2001. 108:S95-S98) and Weinrich et al. (Hybridoma. 1996, 15;2:109-116. Reference C68 in IDS).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Reff et al. teach that several approaches have been used to make antibody better tolerated in human, including (1) humanization approach where the original CDRs and a few key residues that impacted antigen binding were grafted from murine antibody onto a human antibody of similar structure; (2) human antibody approach using transgenic mice where the murine Ig genes have been replaced with human IgG genes (see entire document, particularly pages 26-28). Further, Reff et al. teach smaller versions of antibodies such as single chain antibody, antibody fragments including F(ab) and F(ab')₂ have been made to achieve better penetration of the avascular tumors (e.g. see pages 30-32, in particular).

Reff et al. do not teach humanized or human anti-Fc γ RIIB specific antibody, single chain antibody and its fragments.

However, targeting Fc γ RIIB for therapeutic advantages was well known in the art at the time the invention was made. For example, Ott et al. teach Fc γ RIIB mediated inhibitory signaling is important in regulating immune response because Fc γ RIIB-deficient mice exhibit enhanced antibody production and autoimmunity (see entire document, particularly pages S95-S96). Further, Ott et al. conclude that the development of therapeutics that specifically target Fc γ RIIB may be effective in the treatment of a variety of immunologic disorders (e.g. see Summary on page S97, in particular).

The teachings of Weinrich et al. have been discussed, *supra*, and teach method of making anti-Fc γ RIIB specific antibody.

Therefore, it would have been obvious to the ordinary artisan at the time the invention was made to make humanized or human anti-Fc γ RIIB specific antibody, its fragments, and single chain antibody. The ordinary artisan would have been motivated to do so for human therapies because the inhibitory Fc γ RIIB is a potential target for treating immunologic disorders and humanized or human antibodies are better tolerated in treating human patients; single chain antibodies and antibody fragments penetrate better in avascular tumors.

Given the teachings of Reff et al. regarding the advantages of humanized or human antibody, single chain antibody and antibody fragments, and the teachings of Ott et al. and Weinrich et al. regarding Fc γ RIIB being a potential therapeutic target and the method of making anti- Fc γ RIIB specific antibody, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success of producing humanized or human anti-Fc γ RIIB specific antibody, single chain or antibody fragments that are specific for Fc γ RIIB.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. Claims 1 and 104-107 are rejected under 35 U.S.C. 103(a) as being unpatentable over Presta (US Patent 6,737,056) in view of Ott et al. (J. Allergy Clin. Immunol. 2001. 108:S95-S98) and Weinrich et al. (Hybridoma. 1996, 15;2:109-116. Reference C68 in IDS).

Presta teaches and claims antibodies with modified Fc region for higher affinity to Fc γ RIII and enhanced ADCC (see entire document, particularly columns 5-6 and claims 1-8).

Presta does not teach anti-Fc γ RIIB antibody.

The teachings of Ott et al. and Weinrich et al. have been discussed, *supra*.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the Fc region of the anti-Fc γ RIIB antibody for increased affinity for Fc γ RIII and enhanced ADCC because therapeutics that specifically target Fc γ RIIB may be effective in the treatment of a variety of immunologic disorders and higher affinity and enhanced ADCC can be achieved by modifying amino acids in the Fc region of antibodies.

Given the teachings of Presta regarding modifying Fc region of antibodies to achieve enhanced ADCC, and the teachings of Ott et al. and Weinrich et al. regarding Fc γ RIIB being a potential therapeutic target and the method of making anti- Fc γ RIIB specific antibody, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success of producing Fc modified anti-Fc γ RIIB specific antibody with increased affinity for Fc γ RIII and enhanced ADCC.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1, 9-21, 23, 30-32, 38, 41-43, 81-90, 104-109 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 and 16-20 of copending USSN. 11/305,787.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant and the copending applications claims are drawn to same or nearly the same anti-Fc γ RIIB antibody that specifically binds the extracellular domain of human Fc γ RIIB and/or anti-Fc γ RIIB antibody with Fc modification.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claims 1, 9-21, 23, 30-32, 38, 41-43, 81-90, 104-109 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 9, 10, 14, 15, 53-57, and 63 of copending USSN 11/108,135.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant and the copending applications claims are drawn to same or nearly the same anti-Fc γ RIIB antibody with identical clone name 2B6 that specifically binds the extracellular domain of human Fc γ RIIB and/or anti-Fc γ RIIB antibody with Fc modifications.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. Claims 1, 9-21, 23, 30-32, 38, 41-43, 81-90, 104-109 directed to an invention not patentably distinct from claims 1-13 and 16-20 of commonly assigned USSN 11/305,787; and claims 1-6, 9, 10, 14, 15, 53-57, and 63 of commonly assigned USSN 11/108,135 for reasons stated above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned USSN 11/305,787 and USSN 11/108,135, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

19. No claim is allowed.
20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chun Crowder, Ph.D.

Patent Examiner

March 24, 2006

Phillip Gambel
PHILLIP GAMBEL, PH.D JD
PRIMARY EXAMINER
TC 600
3/27/06

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- 7. Other: _____

Applicant Must Provide:

- An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE